Prevalence of Rickettsial Antibody and Cell-mediated Reaction in Cynomolgus Monkeys (*Macaca fascicularis*)[1,2]

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Summary | Serologic studies on feral, colony-held cynomolgus monkeys indicated that 61% reacted to *Coxiella burnetii* antigens, and 36% reacted to *Rickettsia conorii* antigens. The results suggest that a high percentage of cynomolgus monkeys have been exposed to these organisms.

Key Words | *Coxiella burnetti* — Q fever — *Rickettsia conorii* — *Macaca*

The occurrence of antibodies to various rickettsiae in nonhuman primates has been reported (1–4). Approximately 42% of chimpanzees, 50% of baboons, and 25% of rhesus monkeys tested had complement fixing antibodies to *Coxiella burnetii*; however, only 5% of cynomolgus monkeys had detectable antibodies. Since the cynomolgus monkey (*Macaca fascicularis*) is being employed more extensively in biomedical research due to the limited supplies of rhesus monkeys, additional screening for prior exposure is essential.

This study was carried out to confirm and amplify studies by others (2,3) on the prevalence of antibodies to *C burnetii* and *Rickettsia conorii* in cynomolgus monkeys. Seventy young adult monkeys of both sexes were tested. Animals were in captivity for approximately 2 years and were housed singly.

Serum antibody activity against phase I and II *C burnetii* and *R conorii* was measured by indirect immunofluorescence (5) and microagglutination tests (6). The sensitivity and specificity of these tests have been well established. The lymphocyte transformation test was performed as previously described (7). Titers of ≥ 1:8 in the indirect immunofluresc-ence and microagglutination tests or a stimula-

tion index of >2.0 in the lymphocyte transformation tests were considered significant.

Results in Table 1 show that 18 of 50 (36%) cynomolgus monkeys tested had detectable antibody to *R conorii* or increased lymphocyte blastogenesis. All animals that were positive by the lymphocyte transformation test were negative by indirect immunofluorescence and microagglutination tests. Only one monkey was positive by both of the latter two tests. Antibody titers ranged from 1:8 to 1:64.

Table 1

Antibody and lymphocyte transformation responses of 50 cynomolgus monkeys to *Rickettsia conorii*

Tests	Number monkeys positive
Lymphocyte transformation only	9
Microagglutination only	6
Indirect fluorescence assay only	2
Indirect fluorescence assay + Microagglutination	1
Total	18

The antibody and lymphocyte transformation responses of cynomolgus monkeys to *C burnetii* are shown in Table 2. Forty-three of 70 (61%) animals tested had either positive lymphocyte transformation, microagglutination, or increased lymphocyte responsiveness. Of the nine that were positive by indirect immunofluorescence assay, all had agglutinins to phase II and one had them to both phase I and

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Table 2

Antibody and lymphocyte transformation responses of 70 cynomolgus monkeys to *Coxiella burnetii*

Tests	Phase I only	Phase II only	Both Phases	Total
		Antigen		
Indirect immunofluorescence only	0	8	1	9
Microagglutination only	0	7	4	11
Lymphocyte transformation only	1	0	9	10
Indirect immunofluorescence + Microagglutination				5
Indirect immunofluorescence + Lymphocyte transformation				4
Indirect immunofluorescence + Microagglutination + Lymphocyte transformation				2
Total				43

II. All 11 monkeys positive by the microagglutination test had phase II agglutinins and four had both phase I and II agglutinins. Nine of the 10 animals that had a positive lymphocyte transformation assay had increased lymphocyte blastogenesis with phase I and II antigens, and one with phase I antigen alone. Only two of 43 positive monkeys were positive by all three tests. Antibody titers ranged from 1:8 to 1:128.

Our findings suggest that cynomolgus monkeys previously have been exposed to *C burnetii* and *R conorii*. These monkeys are generally captured in the wild from Malaysia, Indonesia, and the Philippines. Previous studies have shown that *C burnetii* (8) and *R conorii* (9) are endemic in these areas. Our findings indicate the validity of the hypothesis proposed by others that there may be infection occurring in the wild due to *R conorii* (3).

The complement fixation test has been the method of choice in screening for *C burnetii* antibody, but the microagglutination test yields similar results. The lymphocyte transformation assay, which is frequently used as an *in vitro* correlate of cell-mediated immunity, is a sensitive and specific measure of prior exposure to rickettsiae at a time when antibody can no longer be detected (10). Therefore, this test can be used effectively as a screening technique to detect previous exposure. Although serum antibody cross-reactions may occur with *R conorii, R akari, R sibirica,* and *R rickettsii,* the last three rickettsiae are not usually found in the geographic area where the cynomolgus monkeys were obtained.

There was a lack of correlation between the indirect immunofluorescence test, the microagglutinin test, and the lymphocyte transformation assay. At this time we have no explanation for the varied responses.

The results of this study suggest that a high percentage of cynomolgus monkeys have been exposed to *C burnetii* and *R conorii* in nature. Therefore, investigators should develop baseline profiles of cynomolgus monkeys before beginning biomedical research in rickettsial diseases.

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